REMARKS

Claims 27-40 and 42-45 are canceled. Claims 41 and 46 are currently amended. Claims 47-65 are new.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Claim Objections

Claims 41 and 46 were objected to by the Examiner for depending upon withdrawn claims and for including an acronym, which was not initially spelled out. Claims 41 and 46 are currently amended. Reconsideration is urged.

II. The Rejection of Claim 41 under 35 U.S.C. 112, first paragraph (enablement)

Claims 41 stands rejected under 35 U.S.C. 112 because the specification does not reasonably provide enablement for methods of making or enhancing the secretion of a protein of interest by cultivating cells expressing MrgA wherein the protein is expressed in any kinds of cells. Claim 41 is currently amended. Accordingly Applicants have been fully responsive to the Examiners rejection. Reconsideration is urged.

Notwithstanding the above amendments, Applicants note the following:

It is well settled that "[t]he first paragraph of section 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). Moreover, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of section 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 169 U.S.P.Q. at 369.

“The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art ... The test is not quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation

should proceed to enable the determination of how to practice a desired embodiment of the invention claimed ..." *Ex parte Jackson*, 217 U.S.P.Q. 804 (Bd. Pat. App. 1982).

It is also well settled that an assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974). See also *U.S. v. Telectronics*, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974); *Ex parte Hitzeman*, 9 U.S.P.Q.2d 1821 (BPAI 1988).

Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

Applicants submit that the specification enables the claimed invention. The claimed invention is directed to a method for enhancing secretion of a protein of interest, the method comprising expressing the protein in a progeny cell derived from a parent cell. The Office has concede that the specification is enabled for a method of making/enhancing the secretion of a protein of interest by cultivating cells from the genus of Bacillus wherein a progeny cell is derived from a parent cell and wherein said progeny cell encodes at least an MrgA protein and wherein the cells are derived from (and cultivated) the genus Bacillus. Applicants note that the specification also contains various examples. Further the specification discloses on page 11 that the present disclosure relates to recombinant host cells. Such cells are similar in that they can be used in the recombinant production of proteins of interest. Moreover, the specification discloses on page 16, that the choice of host cell will to a large extent depend upon the gene encoding the polypeptide and its source. The specification also discloses that the host cell may be a unicellular microorganism, e.g., a prokaryote, or a non-unicellular microorganism. e.g., a eukaryote. Useful unicellular cells are bacterial cells such as gram positive bacteria. Further the specification includes a detailed description providing extensive disclosure of how to produce the proteins of interest to one of skill in the art.

Moreover, the specification contains an extensive disclosure of how to produce the various cells. For example, the specification discloses that the cells can be cultivated by well known methods such as cultivated in a nutrient medium suitable for production of the polypeptide using methods known in the art. See page 18, lines 34-35. For example, the cell may be cultivated by shake flask cultivation, small-scale or large-scale fermentation (including

continuous, batch, fed-batch, or solid state fermentations) in laboratory or industrial fermentors performed in a suitable medium and under conditions allowing the polypeptide to be expressed and/or isolated. See Specification at page 18, lines 36-37 to page 19, lines 1-2.

It would be routine for one of ordinary skill in the art to produce each cell and test for recombinant characteristics of claim 41.

This evidence establishes that the specification enables the claimed invention. Application of the *Wands* factors to these facts further supports the conclusion that the claims are enabled. First, the present invention is in the field of molecular biology. The *Wands* court has already held that the level of skill in this art is high. *Wands*, 858 F.2d at 740. Second, the specification provides an extensive disclosure for producing the claimed cells. Third, as in *Wands*, the methods of making the claimed cells and screening for the recombinant nature there are known in the art. Fourth, the specification provides working examples of several many different strains of *Bacillus subtiilis*. Fifth, given the extensive guidance given in the specification and the high level of skill in the art, the experimentation involved to produce other cells within the scope of the claims is routine and well within the skill of those in the art. As held by the *Wands* court, "The test is not merely quantitative since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experiment should proceed." *Id.* at 737.

The present disclosure discloses the cells the present invention, and shows, *inter alia*, suitable cells. While some experimentation might be necessary to identify other non-exemplified cells, such experimentation "would not be undue and certainly would not 'require ingenuity beyond that expected of one of ordinary skill in the art.'" (See *Angstadt*, 190 U.S.P.Q. at 218). Certainly, there is no evidence of record to the contrary.

For the foregoing reasons, Applicants submit that Claim 41, as amended, overcomes this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 41 and 46 under 35 U.S.C. 112, first paragraph (enablement)

Claims 41 and 46 stand rejected under 35 U.S.C. 112 because the specification does not reasonably provide enablement for methods utilizing progeny cells expressing functional homologues of MgA and/or any or all DNA segments linked to said homologues; or progeny cells that have been "mutated with respect to the parent cell" and which said progeny cell produces

more MrgA protein than the parent cell. Claims 41 and 46 are currently amended. Reconsideration is urged.

IV. The Rejection of Claims 41 and 46 under 35 U.S.C. 112, first paragraph (written description)

Claims 41 and 46 stand rejected under 35 U.S.C. 112 for containing subject matter which was not described in the specification in such a way as to reasonably convey possession of the claimed invention. The Examiner notes that the claims are drawn to methods of enhancing secretion of proteins of interest or recovering proteins of interest by using progeny cells that express a MrgA protein, MrgA functional homologues or have progeny cells mutated with respect to the parent cell. The Examiner alleges that the MrgA protein is not known. Applicants have amended claims 41 and 46, thus have fully responded to the Examiner. Reconsideration is urged in light of the amendments above. Notwithstanding these amendments, Applicants note the following:

The written description requirement of the Patent Code is fulfilled when the patent specification describes the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See Vas-Cath, Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See In re Marzocchi, 169 USPQ 367 (CCPA 1971).

Under this standard, any conclusion that the specification requires more than SEQ ID NO:2 is incorrect. The specification discloses, and one skilled in the art would clearly recognize, that the scope of the present invention includes MrgA protein, including but not limited to MrgA protein comprising an amino acid sequence which is at least 70% identical to the MrgA protein of SEQ ID NO:2. See page 17, lines 31-35.

Examples of MrgA proteins falling within the scope of the claimed invention include, but are not limited to MrgA proteins comprising an amino acid sequence which is at least 70% identical to the amino acid sequence shown in SEQ ID NO:2; preferably at least 75%, 80%, 85%, 90%, 95%, 97% or even 99% identical to the amino acid sequence shown in SEQ ID NO:2. Accordingly many MrgA proteins are clearly envisioned by an artisan once apprised of Applicants' invention. Accordingly, an artisan would reasonably conclude that Applicants were not only in possession of the MrgA proteins including the protien of SEQ ID NO: 2, but also that Applicants had possession of highly related proteases, as specified by the claims. Indeed, based on the high level of skill in

the art, the phrase “MrgA proteins” itself conveys to the artisan that Applicants were in possession of the claimed invention.

Notwithstanding the above, the Examiner has not provided sufficient evidence or reasoning to rebut that the specification provides an adequate written description for highly related MrgA proteins. In this regard, the Examiner contends that a number of additional representative species are required to be disclosed. However, given the high degree of relatedness in the claims (*i.e.,* the characterization as "MrgA protein") an extremely high degree of predictability exists as to the structure and function of proteases falling within the claims.

Therefore, Applicants respectfully submit that the specification contains a sufficient description of the structural and functional characteristics of the claimed proteases to fulfill the requirements of 35 U.S.C. 112. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

V. The Rejection of Claims 41 and 46 under 35 U.S.C. 102(b).

Claims 41 and 46 were rejected under 35 U.S.C. 102(b) as being anticipated by Chen *et al.* (Mol. Micro., 1995) (hereinafter simply referred to as "Chen"). Claims 41 and 46 are currently amended. Nowhere does Chen describe a progeny cell producing greater amounts of the claimed MrgA than the parent cell, and the progeny cell producing greater amounts of protein of interest than the parent cell. Reconsideration is urged.

VI. New Claims

New claims are presented. No new matter is added. Should any additional fees be due the USPTO is authorized to charge the Deposit Account of Novozymes North America, Inc. *i.e.*, Deposit Account No. 50-1701.

VII. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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